Remarks

Applicant appreciates the thorough examination of the present application as evidenced by the Office Action dated December 23, 2002 (the Action). Claims 1-16 are pending in the present application. Claims 1-16 stand rejected under 35 U.S.C. § 112. Claims 1-16 also stand rejected under 35 U.S.C. § 103.

Claim 1 has been amended to include the recitation "having a hydroxypropyl cellulose content in the range from 5 to 16 % by weight." Support for the amendment to claim 1 can be found in the present application at page 6, lines 1-3, among other places. The concerns raised by the Examiner are addressed below as set forth in the Action.

I. Claim Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 1-16 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. The Examiner has objected to the term "low-substituted" as being a relative term.

Applicant has amended claim 1 to recite that the low-substituted hydroxypropyl cellulose is one "having a hydroxypropyl cellulose content in the range from 5 to 16 % by weight." Thus, Applicant submits that claim 1 and claims 2-16, which directly or indirectly dependent therefrom, are not indefinite under 35 U.S.C. § 112, second paragraph, and respectfully requests that this rejection be withdrawn.

II. Claim Rejections Under 35 U.S.C. § 103

Claims 1-16 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over PCT published application WO 98/53798 (Shimizu) and further in view of U.S. Patent No. 3,852,421 to Koyanagi et al. (Koyanagi et al.). Applicant respectfully traverses this rejection.

Applicants note that in order to establish a *prima facie* case of obviousness, three basic criteria must be met. First, the prior art reference or combination of references must teach or suggest all the claim recitations. *See In re Wilson*, 165 U.S.P.Q. 494 (C.C.P.A. 1970). Second, there must be some suggestion or motivation, either in the references

themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings in order to arrive at the claimed invention. *See In re Oetiker,* 24 U.S.P.Q.2d 1443, 1446 (Fed. Cir. 1992); *In re Fine*, 837 F.2d at 1074; *In re Skinner*, 2 U.S.P.Q.2d 1788, 1790 (Bd. Pat. App. & Int. 1986). Third, there must be a reasonable expectation of success. *See* M.P.E.P. § 2143.

The present invention is directed to a base material for dry direct tableting which is obtained by impregnating low-substituted hydroxypropyl cellulose having a hydroxypropyl cellulose content in the range from 5 to 16 % by weight with a sugar or a sugar alcohol and then drying the product resulting therefrom, as recited in currently amended claim 1.

In contrast, Shimizu is directed to "a solid preparation which comprises (i) a pharmaceutically active ingredient, (ii) one or more water-soluble sugar alcohols selected from the group consisting of sorbitol, maltitol, reduced starch saccharide, xylitol, reduced palatinose and erythritol, and (iii) low-substituted hydroxypropyl cellulose having hydroxypropyl group contents of 7.0 to 9.9 percent by weight." Abstract. Thus, Shimizu is not directed to a base material for dry direct tableting. Moreover, Shimizu is not directed to a base material for dry direct tableting that is obtained by impregnating low-substituted hydroxypropyl cellulose having a hydroxypropyl cellulose content in the range from 5 to 16 % by weight with a sugar or a sugar alcohol and then drying the product resulting therefrom. Instead, Shimizu proposes a complete solid pharmaceutical preparation that comprises, among other things, a low-substituted hydroxypropyl cellulose having hydroxypropyl group contents of 7.0 to 9.9 percent by weight.

Although the solid preparation of Shimizu comprises one or more water-soluble sugar alcohols, Shimizu does not teach or suggest using the sugar alcohol to impregnate the low-substituted hydroxypropyl cellulose component of the Shimizu preparation. Applicant respectfully submits that one of ordinary skill in the art to which the present invention pertains would not rely upon the Shimizu reference proposing a mere combination of components yielding a solid pharmaceutical preparation, in order to arrive at a base material for dry direct tableting that is obtained by impregnating low-substituted hydroxypropyl

cellulose having a specific hydroxypropyl cellulose content with a sugar or a sugar alcohol and then drying the product resulting therefrom.

Thus, where the Action states that "the instant claims differ from the Shimizu reference by claiming that the base material is for dry direct tableting" (Action, page 3), it is clear that the claims of the present invention are vastly different from the proposals of Shimizu where Shimizu fails to teach or suggest a base material for dry direct tableting which is obtained by impregnating low-substituted hydroxypropyl cellulose having a hydroxypropyl cellulose content in the range from 5 to 16 % by weight with a sugar or a sugar alcohol and then drying the product resulting therefrom, as recited in currently amended claim 1.

The Action further cites Koyanagi et al. for the proposition that "[i]t would have been obvious to one of ordinary skill in the art at the time the invention was made to use the low substituted hydroxypropyl cellulose composition of the Shimizu reference for dry direct tableting in view of the recognition in the art, as evidenced by the Koyanagi et al. patent, that a low substituted hydroxypropyl cellulose composition is excellent as a shaping agent and as a binder for forming tablets." Action, page 5. Applicant respectfully disagrees with this assertion.

As noted above, Shimizu does not teach or suggest a base material for dry direct tableting which is obtained by impregnating low-substituted hydroxypropyl cellulose having a hydroxypropyl cellulose content in the range from 5 to 16 % by weight with a sugar or a sugar alcohol and then drying the product resulting therefrom, as recited in currently amended claim 1. The missing recitations are not supplied by Koyanagi et al. Koyanagi et al. merely proposes an excipient that comprises hydroxy alkyl cellulose or hydroxy alkyl alkyl cellulose for shaping medicaments into a solid body that can be disintegrated in the human body. *See* col. 1, lines 9-11. Koyanagi et al. does not teach or suggest a base material for dry direct tableting that is obtained by impregnating low-substituted hydroxypropyl cellulose having a hydroxypropyl cellulose content in the range from 5 to 16 % by weight with a sugar or a sugar alcohol and then drying the product resulting therefrom.

At page 9, line 21 through page 10, line 14, the present application notes the following:

> A powder obtained simply by granulating low-substituted hydroxypropyl cellulose with the aid of water and drying the resulting granular material shows an improvement in flowability. However, this powder is reduced to finer particles as a result of shrinkage on drying. Moreover, this powder is reluctant to deformation in response to the force applied during tableting, thus showing a reduction in binding power. However, in the product of the present invention which is obtained by impregnating low-substituted hydroxypropyl cellulose with a sugar or a sugar alcohol and then drying it, the low-substituted hydroxypropyl cellulose is dried after the sugar or sugar alcohol is introduced into its interstices formed as a result of swelling by water. Consequently, it is believed that the shrinkage of the low-substituted hydroxypropyl cellulose on drying is suppressed. Moreover, owing to the presence of the interstitial sugar or sugar alcohol, the low-substituted hydroxypropyl cellulose easily deforms in response to the force applied during tableting and can hence retain its binding power.

Thus, conventional tableting formulation, as proposed by both Shimizu and Koyanagi et al., does not provide the improved product as disclosed in the present application and as recited in claim 1 and claims dependent therefrom. Consequently, where the Action states that "process limitations cannot impart patentability to a product that is not patentably distinguished over the prior art" (Action, page 4), Applicant respectfully submits that for the reasons discussed above, the base material for dry direct tableting which is obtained by impregnating low-substituted hydroxypropyl cellulose having a hydroxypropyl cellulose content in the range from 5 to 16 % by weight with a sugar or a sugar alcohol and then drying the product resulting therefrom as recited in currently amended claim 1, is patentably distinct from the product provided by Shimizu alone or in combination with Koyanagi et al.

Moreover, Applicant respectfully submits that there is no motivation for one skilled in the art to which the present invention pertains to combine Shimizu and Koyanagi et al. Even if these references were combined, one skilled in the art to which the present invention pertains would not arrive at the present invention in view of the missing recitations that are not provided by either reference. As such, there is clearly no reasonable expectation of success of arriving at the present invention based upon the disclosure of Shimizu alone or in combination with Koyanagi et al.

Therefore, where the cited references fail to disclose all the claim recitations of the present invention, fail to suggest the modification of the references or the combination of reference teachings in order to arrive at the claimed invention and lastly, fail to provide a reasonable expectation of success, the Examiner has failed to establish a *prima facie* case of obviousness.

Accordingly, Applicant respectfully submits that claims 1-16 are patentable under 35 U.S.C. § 103(a) over Shimizu alone, or in combination with Koyanagi et al., and requests that this rejection be withdrawn.

III. Conclusion

In view of the foregoing remarks, Applicants respectfully request that all outstanding rejections to the claims be withdrawn and that a Notice of Allowance be issued in due course. Any questions that the Examiner may have should be directed to the undersigned, who may be reached at (919) 854-1400.

Respectfully submitted,

Shawna Cannon Lemon
Registration No. P-53,888

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I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, Washington, DC 20231, on March 24, 2003.

Vickie Diane Prior
Date of Signature: March 24, 2003